

ACTION: Notice.

SUMMARY: This notice announces receipt of applications to register pesticide products containing active ingredients not included in any previously registered products pursuant to the provisions of section 3(c)(4) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended.

DATES: Written comments must be submitted by February 13, 1995.

ADDRESSES: By mail, submit written comments identified by the document control number [OPP-30378] and the registration/file number, to: Public Response and Program Resources Branch, Field Operations Divisions (7506C), Office of Pesticide Programs, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460. In person, bring comments to: Environmental Protection Agency, Rm. 1132, CM #2, 1921 Jefferson Davis Hwy., Arlington, VA.

Information submitted as a comment concerning this notice may be claimed confidential by marking any part or all of that information as "Confidential Business Information" (CBI). Information so marked will not be disclosed except in accordance with procedures set forth in 40 CFR part 2. A copy of the comment that does not contain CBI must be submitted for inclusion in the public record. Information not marked confidential may be disclosed publicly by EPA without prior notice. All written comments will be available for public inspection in Rm. 1132 at the address given above, from 8 a.m. to 4 p.m., Monday through Friday, excluding holidays.

FOR FURTHER INFORMATION CONTACT: By mail: Janet L. Andersen, Acting Director, Biopesticides and Pollution Prevention Division (7501W), Office of Pesticide Programs, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460. Office location and telephone number: Rm. CS51B6, Westfield Building North Tower, 2800 Crystal Drive, Arlington, VA 22202, (703-308-8712).

SUPPLEMENTARY INFORMATION: EPA received applications as follows to register pesticide products containing active ingredients not included in any previously registered products pursuant to the provisions of section 3(c)(4) of FIFRA. Notice of receipt of these applications does not imply a decision by the Agency on the applications.

Products Containing Active Ingredients Not Included In Any Previously Registered Products

1. File Symbol: 56336-RT. Applicant: Consep, Inc., 213 Southwest Columbia St., Bend, OR 97702. Product name: Consep SPRA4 Peach Twig Borer Pheromone Sprayable. Insecticide. Active ingredients: (*E*)-5-decenyl acetate at 46.20 percent and (*E*)-5-decenol at 9.60 percent. For tree nut crops and other crops; for the control of peach twig borer.

2. File Symbol: 56336-RL. Applicant: Consep, Inc. Product name: Checkmate Peach Twig Borer (PTB) Technical Pheromone. Insecticide. Active ingredients: (*E*)-5-decenyl acetate at 77 percent and (*E*)-5-decenol at 16.00 percent. For use in manufacturing or formulation only.

3. File Symbol: 56336-RA. Applicant: Consep, Inc. Product name: Check-mate PTB Dispenser. Insecticide. Active ingredients: (*E*)-5-decenyl acetate at 7.92 percent and (*E*)-5-decenol at 1.65 percent. For tree nut crops and other crops; for the control of peach twig borer.

Notice of approval or denial of an application to register a pesticide product will be announced in the **Federal Register**. The procedure for requesting data will be given in the **Federal Register** if an application is approved.

Comments received within the specified time period will be considered before a final decision is made; comments received after the time specified will be considered only to the extent possible without delaying processing of the application.

Written comments filed pursuant to this notice, will be available in the Public Response and Program Resources Branch, Field Operation Division office at the address provided from 8 a.m. to 4 p.m., Monday through Friday, except legal holidays. It is suggested that persons interested in reviewing the application file, telephone the FOD office (703-305-5805), to ensure that the file is available on the date of intended visit.

Authority: 7 U.S.C. 136.

List of Subjects

Environmental protection, Pesticides and pests, Product registration.

Dated: January 6, 1995.

Janet L. Andersen,

Acting Director, Biopesticides and Pollution Prevention Division, Office of Pesticide Programs.

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[OPP-30000/59; FRL-4918-8]

Propoxur (Baygon, Sendran); Proposed Decision Not to Initiate a Special Review

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice; Proposed Decision Not To Initiate a Special Review.

SUMMARY: This Notice announces EPA's proposed decision not to initiate a Special Review of the insecticide propoxur (Baygon, Sendran; 2-isopropoxy-phenyl-*N*-methylcarbamate). The Special Review was originally proposed on the basis of potential carcinogenic risks to applicators and home residents from the registered uses. After evaluating new exposure and carcinogenicity data, and in light of voluntary cancellation and label amendment actions which eliminated those uses posing the greatest concern, EPA believes that the estimated risks do not warrant initiation of Special Review. **DATES:** Written comments must be received on or before March 14, 1995.

ADDRESSES: Submit three copies of written comments, bearing the document control number "OPP-30000/59," by mail to: Public Response and Program Resources Branch, Field Operations Division (7506C), Office of Pesticide Programs, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460. In person, bring comments to: Rm 1132, Crystal Mall Building #2, 1921 Jefferson Davis Highway, Arlington, VA 22202.

Information submitted in any comment concerning this Notice may be claimed confidential by marking any part or all of that information as "Confidential Business Information" (CBI), and so marking on the cover of each copy submitted. Information so marked will not be disclosed except in accordance with procedures set forth in 40 CFR part 2. Two complete copies should be submitted with section(s) claimed CBI clearly marked, and numbered consecutively throughout the text. The third copy should have the claimed CBI section(s) excised and numbered consecutively (as in the two complete copies) without modifying the remaining text. The propoxur public docket has been open for public inspection since February 1992. An index of propoxur documents, information supporting this proposed action and any submitted comment or part of a comment is available for public inspection and copying in the Public Docket, Rm. 1132 at the Virginia address given above. Office hours are from 8

a.m. to 4:30 p.m., Monday through Friday, except legal holidays.

FOR FURTHER INFORMATION CONTACT: By mail: Ann Sibold, Review Manager, Environmental Protection Agency (7508W), 401 M St., SW., Washington, DC 20460. Office location and telephone number: 2800 Crystal Drive, 3rd Floor, Arlington, VA 22202, (703) 308-8033.

SUPPLEMENTARY INFORMATION: EPA announces its proposed decision not to initiate a Special Review of propoxur. EPA has re-evaluated the concerns raised in its March 22, 1988 preliminary notification letter to registrants (Refs. 1), along with other relevant information and the regulatory actions taken since the preliminary notification. Based on this re-evaluation, EPA has determined that a Special Review of propoxur is not warranted at this time.

I. Introduction

A. Chemical Background

Propoxur is the common name for 2-isopropoxy-phenyl-*N*-methylcarbamate, a carbamate insecticide for the control of insects and other arthropods inside and outside of buildings and on pets. The holders of the two U.S. technical registrations of propoxur, Baygon and Sendran, are Miles Inc., Agriculture Division (formerly Mobay Corp., Agricultural Chemical Division), and Miles Inc., Animal Health Division (formerly Mobay Corp., Animal Health Division) respectively. Miles Inc. is a subsidiary of Bayer, AG, Germany. Approximately 100 companies hold active registrations for intermediate and/or end-use products in which propoxur is an active ingredient (a.i.). There are approximately 200 registrations for formulations containing propoxur, including 2 technical products, Baygon (96 percent) and Sendran (94 percent), and 19 formulation intermediates.

End-use propoxur products provide contact kill and residual control of a wide variety of common indoor insects, such as ants and cockroaches. Propoxur formulations are also sold for the control of fleas and ticks on pets. In addition, propoxur-containing products are sold for limited outdoor uses. For example, it is used in wasp and hornet sprays, and application to and around building surfaces and foundations, patios, driveways, and sidewalks. Propoxur products are sold as wettable powders, emulsifiable concentrates, aerosols, total-release aerosol foggers, ready-to-use (RTU) liquids, granular baits, enclosed baits, impregnated or controlled release strips and shelf paper. Wettable powders and emulsifiable concentrates (diluted and mixed with

water) and RTU liquids can be applied using a compressed air sprayer in both household and non-household settings. Pest Control Operators (PCOs) use emulsifiable concentrates, wettable powders, and granular products. Pet-use products are sold as aerosol sprays, collars, and dab-ons. There are a number of propoxur insecticides which contain other active ingredients such as dichlorvos (DDVP), piperonyl butoxide, pyrethrins, allethrin, and *N*-octyl bicycloheptene dicarboximide. EPA estimates that combined indoor and outdoor household uses (applied by both residents and PCOs) account for 80 to 92 percent of total propoxur usage in the United States. PCOs apply approximately 6 percent to 9 percent of the total propoxur used in homes. Residents of single family homes, condominiums and apartments are the primary users of propoxur products sold as aerosols or RTU liquids. There is limited use (up to about 8 percent) of propoxur in commercial establishments.

B. Legal Background

1. *Statute.* A pesticide product may be sold or distributed in the United States only if it is registered or exempt from registration under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) as amended (7 U.S.C. 136 et seq.). Before a product can be registered it must be shown that it can be used without "unreasonable adverse effects on the environment" (FIFRA section 3(c)(5)), that is, without causing "any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of the pesticide" (FIFRA section 2(bb)). The burden of proving that a pesticide meets this standard for registration is at all times on the proponent of initial or continued registration. If, at any time, EPA determines that a pesticide no longer meets this standard for registration or reregistration, the Administrator may cancel the registration under sections 3 or 6 of FIFRA.

2. *Special Review process.* EPA initiates a Special Review when it determines that a pesticide meets or exceeds one or more of the risk criteria set out in the regulations (40 CFR 154.7). The Special Review process is described in 40 CFR part 154, published in the **Federal Register** of November 27, 1985 (50 FR 49015). During a Special Review, EPA: (1) announces and describes EPA's finding that use of the pesticide meets one or more of the risk criteria set forth in 40 CFR 154.7; (2) establishes a public docket; (3) proposes a regulatory decision; (4) solicits

comments from the public on the issues and proposed regulatory decision of the Special Review, and from the Secretary of Agriculture and the FIFRA Scientific Advisory Panel on the Agency's analysis and proposed decision; (5) reviews and responds to all significant comments submitted within the stated time frame; and (6) makes a final regulatory decision based on the risks and benefits associated with each use of the pesticide.

Prior to formal initiation of a Special Review, a preliminary notification is sent to registrants and applicants for registration pursuant to 40 CFR 154.21 announcing that the Agency is considering commencing a Special Review.

If the Agency determines, after issuance of a notification pursuant to 40 CFR 154.21, that it will not conduct a Special Review, it is required under 40 CFR 154.23 to issue a proposed decision to be published in the **Federal Register**. This Notice is being issued under 40 CFR 154.23. A period of not less than 30 days is to be provided for public comment on the Proposed Decision Not To Initiate a Special Review. Subsequent to receipt and evaluation of comments on the Proposed Decision Not To Initiate a Special Review, the Administrator is required by 40 CFR 154.25 to publish in the **Federal Register** a final decision regarding whether or not a Special Review will be conducted.

C. Regulatory Background

1. *Data Call-In (DCI) Notices.* EPA issued DCI Notices to various propoxur registrants in 1987, 1988, 1989, and 1992. Following these DCIs, registrants either voluntarily cancelled or deleted from labels certain uses, as follows: all propoxur-containing dusts; all outdoor uses (except for the following limited uses: application to the exterior of buildings and around foundations, patios, driveways, and sidewalks); ready-to-use (RTU) liquids applied with trigger pump sprayers; and certain pet uses including dips and shampoos. Miles Inc., the registrant of technical propoxur, submitted five acceptable studies that EPA used in its exposure assessments (PCO and post-application exposures from crack and crevice treatments using compressed air sprayers, residential applicator (RA) exposure using aerosol sprays, PCO exposure from granular bait uses, and applicator exposure from pet aerosols).

2. *Notification of registrants.* On March 22, 1988, pursuant to 40 CFR 154.21(a), EPA issued a private ("Grassley-Allen") notification to propoxur registrants that the Agency

was considering a Special Review of propoxur (Ref. 1). EPA was concerned with propoxur's potential cancer risk to applicators when applying propoxur indoors and outdoors, to occupants of treated buildings, and from treating pets with propoxur. EPA's concern was based on a 1984 study which reported increases in the incidences of malignant and benign tumors in the urinary bladders of both male and female rats, an increase in incidence of uterine tumors in female rats, and the early onset and increased incidence of hyperplasia of the urinary bladder in these rats. EPA classified propoxur as a Group B2 (probable human) carcinogen. EPA noted that data from the 1987 DCI would be used to refine estimates of risk, and that the registrants' responses to this notification would be considered in its determination whether to initiate a Special Review.

3. *1990 Notice of Intent to Suspend, and 1991 Settlement Agreement.* On October 15, 1990, EPA sent a Notice of Intent to Suspend (NOITS) to Miles Inc. and the five manufacturing-use producers for failure to comply with the terms of the December 14, 1987 DCI regarding certain exposure studies. The requirements of the 1987 DCI were legally binding only for those companies who received the DCI. As a result, only their products were subject to the NOITS. Miles Inc. requested a hearing concerning the NOITS, and subsequently reached a settlement with EPA on June 28, 1991. The agreement noted that Miles Inc. had recently submitted new studies to address the data requirements for indoor pressurized aerosol and granular bait products. EPA agreed to issue a new DCI requiring end-use registrants to submit exposure studies not committed to by Miles Inc., such as a trigger pump spray study. If no other end-use registrant committed to generate data to support these uses, Miles Inc. would amend its labels for its manufacturing-use products to prohibit the unsupported uses. On August 12, 1991, after accepting the aerosol spray and PCO granular bait studies submitted by Miles Inc., EPA withdrew the NOITS on all of the registered products of manufacturing-use producers which these two studies supported. RTU liquid products applied with trigger-pump sprayers subject to the NOITS remained suspended. Subsequently, all registrants with these products amended their propoxur end-use product labels to delete use of RTU liquids with trigger-pump sprayers.

II. Estimation of Propoxur Cancer Risks to RAs, PCOs, and Residents of Treated Buildings

Since the 1988 notification to registrants that EPA was considering a Special Review of propoxur, the Agency has refined its risk assessments. The current risk assessment is discussed in this unit.

A. Hazard Identification — Carcinogenicity

1. *Animal carcinogenicity studies— a. Rat studies.* In a 1984 2-year rat chronic feeding/carcinogenicity study, propoxur was administered in a standard European diet (Altromin 1321) to SPF Wistar rats, at concentrations of 0, 200, 1,000, or 5,000 ppm propoxur. At the 1-year interim sacrifice, there was an increased incidence of urinary bladder epithelial hyperplasia in the two highest dose groups of male and female rats. There was also a urinary bladder papilloma in 1 of the 10 highest dose males. Animals that died, were moribund, or were sacrificed at term also had dose-related increases in the degree and extent of urothelial hyperplasia. Highly significant increases in urinary bladder papillomas, carcinomas and combined papillomas/carcinomas (67 to 75 percent versus 0 percent in the controls) were observed in male and female rats at the highest dietary exposure level (5,000 ppm) in this study. Bladder tumors are considered to be relatively rare in rodents, especially in the absence of silica crystalline deposits. Additionally, there was an increased incidence of uterine carcinoma (not statistically significant at $p > 0.05$) in females at the highest dose level. However, it appeared that this tumor had a tendency to develop earlier and/or grow more rapidly than the control group. The urinary bladder findings of the 1984 carcinogenicity study were confirmed in a subsequent 2-year study completed in 1988 with female Wistar rats on an Altromin diet. There were significant increases in urinary bladder papillomas and combined papillomas/carcinomas at the three highest dose levels tested (3,000, 5,000 and 8,000 ppm) and in carcinomas at the highest dose level. The dose-related trends for papillomas, carcinomas and combined papillomas/carcinomas were also significant. Also, the observed hyperplasia of the urinary bladder was dose- and time-dependent. However, a significant comparative pairwise increase in uterine tumors was not observed in this study.

b. *Mouse studies.* In a 1982 2-year mouse carcinogenicity feeding study, male and female CF1/W74 mice were

fed propoxur at dose levels up to 6,000 ppm. No adverse effects on the bladder were noted. Similarly, in a 1988 1-year mouse feeding study, where up to 8,000 ppm propoxur in an Altromin diet was administered to female NMRI mice, no histopathological changes were observed. In a 1992 B6C3F1 mouse carcinogenicity/feeding study using up to 8,000 ppm propoxur in an Altromin diet, there was a dose-related increase in bladder epithelial hyperplasia (classified as minimal and diffuse in all instances) at 2,000 and 8,000 ppm (not at 500 ppm), but no indication of any carcinogenic effect involving the urinary bladder. However, the study did show a dose-related trend of increased incidence of hepatocellular adenomas in males.

c. *Other animal studies.* In a 1988 study, female Syrian hamsters were fed up to 8,000 ppm propoxur in an Altromin diet for 1 year without histopathological effects involving the urinary bladder. In a 1984 1-year dog feeding study, no adverse urinary bladder effects were reported using dose levels up to 1,800 ppm. Also, in a 1985 13-week oral gavage study with Rhesus monkeys, no adverse urinary bladder effects were noted after feeding 40 mg/kg/day of propoxur.

2. *Other studies— a. Metabolism and biotransformation.* Miles Inc. has submitted results of a number of biotransformation studies conducted on different mammalian species (rat, mouse, hamster, monkey, and human). Propoxur is extensively metabolized (more than 10 metabolites have been identified) and many of the metabolites are excreted in the urine. Because propoxur is so completely metabolized, there is very little or no parent compound in urine. One of the metabolites is 1,2-dihydroxybenzene ("M1" or catechol). In the rat, approximately 7 percent to 20 percent of propoxur is degraded to catechol. Catechol, at high dose levels administered by gavage, has been shown to induce cancer in the glandular stomach of rats. Three other metabolites of propoxur of structural interest are: 2-isopropoxyphenol ("M2"), 2-isopropoxylphenyl-hydroxy-methylcarbamate ("M5"), and 1-hydroxy-2-isopropoxy-4-nitrobenzene ("M9A"). "M9A" has a nitro-group added to the phenyl ring of metabolite "M2," and Miles Inc. has proposed that it is formed in the stomach. In human data (Ref. 2), the glucuronide conjugate of "M2" was the predominant metabolite found, with trace levels of "M9A." Based on the Agency's current knowledge, none of the metabolites

would appear to be of carcinogenic concern.

b. *Mutagenicity.* Propoxur and its metabolites, including catechol, have not been shown to produce detectable gene mutations, with the exception of "M5" (equivocal or weakly positive in the Ames assay for *Salmonella typhimurium* strain TA1535). While propoxur appears to give no indications of clastogenic activity in *in vitro* studies submitted by Miles Inc., one published study shows increased incidence of sister chromatid exchange and micronuclei in human lymphocytes following *in vitro* exposure to propoxur. Propoxur also induces S-phase mitosis in bladder epithelial cells suggesting an effect on cell proliferation. The "M1" metabolite, catechol, has been shown to be genotoxic in several published studies, including *in vivo* tests, primarily via a clastogenic mechanism. The presence of the "M9A" metabolite suggests a possible nitrosation mechanism; the N-nitroso derivative of propoxur is a known mutagenic compound. Overall, the indications are that there is, at most, only weak genotoxicity associated with propoxur and/or its metabolites. It is noteworthy that dietary exposure to propoxur has been shown to result in an increased incidence of S-phase in rat urinary bladder epithelial cells (not a genotoxic effect) suggesting that the rat urinary bladder tumors may originate from increased cell proliferation.

c. *Effects of diet and urinary pH on the bladder.* Miles Inc. has submitted a number of studies relating to the effects of diet and urinary pH on the bladder. In a 15-week feeding study, female Wistar rats received 8,000 ppm propoxur in Altromin diet, with or without addition of 2 percent ammonium chloride. Without the ammonium chloride, the urinary pH was more basic by approximately 2 pH units. At termination, hyperplasia of the urinary bladder was present in 8/14 rats not receiving ammonium chloride and in 1/15 rats receiving it. In two other studies with rats given a casein semi-synthetic diet (No. 1/0) and propoxur at 8,000 ppm for 4.8 or 14 weeks, and at 3,000 or 8,000 ppm propoxur for 100 weeks, no histopathologic changes in the urinary bladder were reported. These studies appear to support Miles Inc.'s position that development of the urinary bladder hyperplasia (and subsequent tumor occurrence in rats) is associated not only with administration of propoxur but also with the diet and possibly its effects on urinary pH.

3. *Findings and recommendations of EPA's Scientific Advisory Groups.* In the September 4, 1986 Peer Review of

propoxur, the Peer Review Committee reviewed the evidence of carcinogenicity of propoxur from the 1984 rat feeding/carcinogenicity study, and other toxicological data on the chemical. The Peer Review Committee reviewed the carcinogenic potential for classification, and concluded that there was sufficient evidence of carcinogenicity to classify propoxur to Group B2 (Probable Human Carcinogen). The classification was supported by the unusually high incidence of bladder neoplasia, the relative rarity of the bladder tumor in rats, early onset of hyperplasia and papilloma of the bladder, and the somewhat uncommon finding of bladder tumors in the absence of crystalline (usually silica) deposits.

In the second Peer Review of propoxur held on December 6, 1990, the Carcinogenicity Peer Review Committee reviewed the evidence for the Group C Classification of propoxur by the Carcinogen Assessment Group of EPA's Office of Research and Development. The Peer Review Committee agreed to defer discussion of the classification of propoxur until the data from the 1988 rat carcinogenicity study had been reviewed.

In the October 3, 1991 third Peer Review of Propoxur, the Carcinogenicity Peer Review Committee concluded "that there was insufficient evidence to change the classification of propoxur (Group B2 carcinogen) and method of quantification" at this time. However, the Committee stated that if a species- and diet-specific effect could be established, and if the genotoxic mode of action were dismissed for propoxur, then "the use of the conventional low-dose quantitative risk assessment method (Q_1^*) might not be appropriate." The Committee suggested that "studies designed to further investigate the mechanism of action and genotoxic potential" of propoxur be performed. Specifically, the Committee suggested a re-cutting of the bladder sections and that a pathologist (with expertise in bladder neoplasia) read these and re-read the original bladder slides from the 1988 female rat study. The Committee suggested that a pathologist look at sections from all groups for uterine pathology from the same study. The Agency also suggested historical control data from the registrant's testing facility and information on the diet composition (Altromin 1321 compared to other diets). In addition, to better understand possible mechanistic considerations and relate them to the Agency's regulatory position on propoxur, Miles Inc. was advised to clarify propoxur's genotoxic

potential and to resolve the discrepancy created by the two dietary regimens.

Miles Inc. has responded, in part, to the suggestions of the third Carcinogenicity Peer Review Committee. The Agency has discussed with the registrant the mechanisms by which the urinary bladder tumors are triggered and the possible relationship of uterine tumors to dietary propoxur. The findings will be evaluated by the Carcinogenicity Peer Review Committee after all the suggested data have been submitted. EPA does not expect that the peer review will conclude that the carcinogenicity of propoxur is a more serious concern than today's document concludes.

4. *Evaluation of carcinogenicity data—Hazard finding.* Following the October, 1991 Peer Review, EPA re-evaluated (Ref. 3) the rat urinary bladder tumor rates from the 1984 2-year feeding study. As there was no statistical evidence of increasing mortality with increasing doses of propoxur, the unit risk estimate could be obtained using a linearized Multi-Stage model for each sex group of rats. The resulting unit risk estimates for both males and females were then combined to obtain a geometric mean. The Agency estimated the human equivalent potency (Q_1^*) of propoxur to be 3.7×10^{-3} (mg/kg/day)⁻¹. The Q_1^* represents the 95 percent upper bound confidence limit of tumor induction likely to occur from a given dose of a carcinogen. It is emphasized, that if the mechanism(s) by which the urinary bladder tumors develop in rats involves a threshold level, and/or if these tumors are species-specific, then the risk to humans would be less than indicated by this Q_1^* .

5. *Uncertainties in propoxur's role in carcinogenesis.* To date, there is no clear indication as to how propoxur produces hyperplasia and tumors. Bladder tumors are rare in rats, particularly in the absence of crystalline (silica) deposits. It has been suggested that silica deposits may in some way participate in bladder tumor formation, especially in the presence of a diet that may alter the pH of urine in the bladder. It is emphasized that there is no indication of silica deposits in the urinary bladders of rats fed propoxur. However, there may be other factors associated with induction of hyperplasia or the formation of tumors, such as enhancement of the cellular response to growth factors. In addition, the role and relative contributions of the parent compound and its metabolites to the process are unknown.

Miles Inc. has taken the position that propoxur is non-genotoxic, and that an "epigenetic" mechanism, such as that

involving dietary exposure to sodium saccharin, is likely to be responsible for the formation of rat urinary bladder tumors in chronic animal feeding studies. Chronic dietary exposure to sodium saccharin at appropriate levels leads to urothelial hyperplasia and subsequent bladder tumors in rats. However, silica microcrystals are found in the urinary bladder of rats fed sodium saccharin and these are absent in rats fed propoxur.

Miles Inc. recently reported on the results of a preliminary scanning electron microscopy study designed to determine if silica crystalline deposits occur in the urinary bladders of propoxur-treated rats and their possible role in inducing hyperplasia and tumors as mediated by the diet and urinary pH. No silica crystalline deposits were observed. The registrant has maintained its previous position of a non-genotoxic mechanism for propoxur-induced cell proliferative response in the rat bladder, but added that propoxur may act like a mitogen (that is, it promotes increased cell division, but does not, by itself, alter cell DNA). It is not known whether a complex interaction of weak or moderate genotoxic activity, cell proliferation and cytotoxicity in the urinary bladder results in tumor formation, or whether cell proliferation alone can cause this effect. Miles Inc. has indicated that it is studying whether there are genotoxic effects in the urinary bladder. In the absence of this information, which might indicate a threshold effect, and for purposes of this risk assessment, EPA has used the linear multistage model that it typically uses.

The Agency has received data from Miles Inc. which indicates the elevated incidence (8/48 or 16.7 percent) of uterine carcinomas observed at 5,000 ppm in a 2-year rat study was within the range (0/50 to 10/50) observed for historical control groups in a series of 32 chronic feeding studies in rats. The overall incidence of uterine carcinomas and/or adenocarcinomas was 163/2,107, or 7.7 percent.

Until propoxur is reviewed again by the Carcinogenicity Peer Review Committee and concludes differently, propoxur remains classified as a B2 carcinogen for which the carcinogenic potency has been quantified at 3.7×10^{-3} (mg/kg/day)⁻¹.

B. Exposure

The estimates of exposure for Pest Control Operators (PCOs), Residential Applicators (RAs), and residents of treated homes are discussed below and displayed in Table 1 below.

1. *Applicator exposure.* The main routes of human exposure to propoxur

are through dermal contact with and inhalation of residues. Residues may be found on surfaces to which propoxur has been applied. However, propoxur may volatilize or evaporate during and following application, and be deposited onto other, untreated interior surfaces of a building. Inhalation exposure occurs from contact with propoxur vapors or dust during and following application of propoxur products. PCOs and RAs are exposed primarily during the mixing, loading, and application of propoxur products to the interior or around the exterior of buildings. Kennel workers and pet owners are exposed while treating animals. Residents of treated buildings are exposed to airborne and surface residues following application. EPA assessed human exposure to propoxur using data obtained from several sources, including studies submitted by Miles Inc. in response to the 1987 DCI, data from the technical literature, and surrogate data. The exposure data and the related estimates are discussed below.

a. *Crack and crevice study of PCO exposure.* Crack and crevice treatments are among the most popular propoxur uses for indoor pest control. In response to the December 14, 1987 Data Call-in (DCI) requirement, Miles Inc. submitted an acceptable crack and crevice study of PCO exposure (Ref. 4), in which Miles Inc. monitored the dermal and inhalation exposures of three PCOs as they treated five homes each. In this study, PCOs used a compressed air sprayer to apply a wettable powder formulation of propoxur, diluted to 1.1 percent active ingredient (a.i.), to cracks and crevices and as a limited broadcast treatment. The PCOs wore chemical-resistant gloves, cotton/polyester coveralls over a long sleeved shirt and long pants, and leather boots. Dermal exposure was monitored using gauze patches inside and outside clothing. Levels of residues on PCOs' hands were measured using an ethanol handwash. Inhalation exposure was measured by using personal sampling devices located in the applicator's breathing zone. (Inhalation exposure was found to be negligible compared to dermal.)

(1) *Wettable powders.* To estimate PCO exposure to wettable powders, EPA supplemented the crack and crevice data with additional assumptions as follows: the average PCO weighs 70 kg, works 8 hours per day over a 20-year working-life of a 70-year life-span, and handles 924 oz. a.i. per year. Dermal absorption was assumed to be 50 percent. Dermal exposure was estimated at 5.2×10^{-3} mg/kg/day (Ref. 5).

(2) *Ready-to-Use (RTU) liquids.* EPA determined that RTU liquid products

are applied at rates similar to the wettable powder formulations, and residues are not expected to be higher or more persistent than those from the wettable powder formulation. For this reason, EPA determined the results of the crack and crevice exposure assessment for wettable powders should be used to estimate PCO exposure during application of RTU liquids (Refs. 5, 6 and 7). Thus, exposure was estimated at 5.2×10^{-3} mg/kg/day.

b. *Granular bait study.* Granular baits are formulated as dry pellets, usually containing 2 percent propoxur. They can be scattered on paper, pasteboards, or on the floor at a rate of about 4 oz per 500 to 1,000 square feet areas. Baits are used near baseboards, in closets, under sinks and refrigerators, around structures, patios, sidewalks and other places where insects may be. Miles Inc. submitted an acceptable study of PCO exposure to granular products. In this study, PCOs wore gloves, long-sleeved shirts, cotton trousers, and baseball caps over normal clothing which consisted of denim or cotton trousers, long-sleeved shirts and shoes while applying 2 percent granular baits by hand to a 2 to 3 foot wide band around driveways, sidewalks, patios, and flower beds, at the prescribed label rate of 4 oz per 1,000 square feet (0.08 oz. a.i./1000 sq. ft.). The granules were applied by three PCOs, each of whom carried a 5 pound carton of the bait in one hand while scattering the material with the other hand. Dermal exposure was measured using gauze patches worn both inside and outside the clothing and on the front of the cap. Hand exposure was measured from an ethanol handwash. Airborne residues were determined by drawing air from the breathing zone through filters using calibrated personal sampling pumps. Propoxur residues were not detected in most of the samples analyzed for dermal or respiratory exposure. Similarly, propoxur was not detected in hand washes after removal of the protective gloves. Because of the large numbers of samples with non-detectable values, EPA determined under these conditions that the exposure would be negligible for PCOs (Refs. 6, 7, and 8).

c. *Aerosol pet spray study.* A number of pressurized aerosol spray products are formulated for use directly on dogs and cats. The amount of a.i. in the products varies from 0.25 percent to 1 percent propoxur. In response to the 1987 DCI requirement, Miles Inc. submitted an acceptable aerosol pet spray study (Ref. 10). In this study, exposures of five workers using a 0.025 percent aerosol spray of propoxur were measured at each of three different

locations as each worker applied the spray to 20 dogs. All treatments were conducted indoors. Each dog was treated for 1 to 2 minutes. The elapsed time for each replicate ranged from 45 to 90 minutes per worker. Each worker wore a shirt with long or short sleeves and pants, but no other protective clothing. Urine was collected from each subject over a 24 hour period and analyzed for the propoxur metabolite isopropoxyphenol (IPP) (This is the same as 2-isopropoxyphenol or M2 discussed in Unit II.A.2.(a) of this document.) After reviewing the literature, EPA concluded that the total absorbed dose of propoxur is determined by adjusting the amount of IPP excreted by the following factors: the percent of propoxur excreted, the percent IPP is of all metabolites, and the relative molecular weights of the parent and the metabolite IPP (Refs. 10, 11, and 12).

(1) *Kennel workers.* An exposure estimate is not presented here because the Agency does not believe pet aerosol products are routinely used by kennel workers. The Agency believes that kennels are more likely to use shampoos or dips because they are more effective in getting rid of fleas and ticks. Shampoos are preferred to other formulations because they wash away dirt, fleas, and ticks in addition to the pesticidal action. Also, they are believed to be easier on the animal. Aerosols and trigger-pump sprays are sometimes used when a pet owner declines to have a pet shampooed or dipped. There are no propoxur shampoos or dips registered, and as noted elsewhere in this document, propoxur may no longer be applied with trigger-pump sprayers.

(2) *Pet owners.* In order to calculate lifetime exposure for pet owner applicators, EPA supplemented the mean exposure data from the aerosol exposure study with the following additional assumptions. Pet owners were assumed to weigh 70 kg, wear long sleeved shirts and long pants during application, and treat 1 dog four times per year over a 70-year lifetime (Refs. 6, 7, 12, 13, and 14). Exposure was estimated at 6.4×10^{-3} mg/kg/day per application day.

d. *Aerosol spray study of Residential Applicator (RA) exposure.* In response to the 1987 DCI, Miles Inc. submitted a study of residential applicator exposure (Ref. 15). In this study, a 16 oz. aerosol can containing 1 percent a.i. was sprayed into cracks, crevices, baseboards, under sinks, and in other places where insects might be found. A total of 15 sets of data were collected. Applicators wore long sleeved shirts, long pants, shoes, and baseball caps.

Dermal exposure data were gathered from gauze patches attached both outside and inside the clothing and on the cap. Hand exposure data were gathered from an ethanol handwash. Respiratory exposure data were gathered from microfilters contained in a cassette attached to the lapel of the applicator.

(1) *RA exposure to aerosols.* EPA used additional assumptions to calculate exposure as follows: the RA weighs 70 kg, breathes 1.7 m^3 of air per hour, uses up the entire can of aerosol with each use, uses four cans per year, and during application wears a short sleeve shirt, shorts, and shoes, which EPA believes is a reasonable clothing scenario. Residues below the level of detection were assumed to be present at one-half the level of detection. The RA was assumed to apply propoxur every year from age 18 to age 70. RAs were exposed for 1 hour per application through dermal and inhalation exposure. (Respiratory exposure estimates were found to be negligible compared to dermal exposure.) Dermal absorption was assumed to be 50 percent because a homeowner applicator is assumed to remain in the residence following application. Exposure was calculated at 2.1×10^{-4} mg/kg/day (Refs 6, 7, 16, 17, 18, and 19).

(2) *Outdoor uses.* EPA also considered RA exposures for outdoor application of propoxur aerosols, which are designed to eradicate hornet and wasp nests around buildings and homes. These insects commonly nest in eaves of buildings and underneath building structures with overhangs. These products are generally equipped with a delivery system that will allow the operator to apply the aerosol at a safe distance from the nest. An applicator of these formulations of propoxur is likely to be exposed for a shorter time than would occur with indoor use products. It is also likely that the volatile formulations would dissipate more quickly than similar formulations used indoors. Thus, the exposure and corresponding risk from outdoor aerosol uses can be expected to be lower than is estimated for those used in indoor treatments (Ref. 15).

(3) *RTU liquid application by RAs.* EPA has used the aerosol spray study to calculate the maximum exposure RAs incur when applying RTU liquids with a compressed air sprayer to cracks and crevices. EPA assumed that the RA would wear a short sleeved shirt, shorts, shoes, and no gloves and would apply an RTU liquid four times per year. Only dermal exposure data were used to calculate exposure, because inhalation was considered to be negligible. Exposure was estimated at 2.1×10^{-4}

mg/kg/day. If the RA applicator wears clothing similar to a PCO, that is, long sleeved shirt, long pants, and gloves, exposure would be less (Refs. 6, 7, 12, 16, 17, 18, 19, 20, and 21).

(4) *Granular products applied by RAs.* Some granular products are registered for use in and around the home (including limited outdoor application to driveways, sidewalks, patios, and foundations). These products are applied indoors by pouring from a paper container into a tray which is then placed under refrigerators, by lightly applying the product to floor under sinks or refrigerators, or by application to cracks and crevices that are inaccessible to children. They are not applied by general broadcast treatment indoors or in large quantities. While there are no quantitative data addressing this use scenario, EPA believes that potential dermal exposure would not exceed that received from an aerosol spray can while wearing a long sleeve shirt and long pants. Respiratory exposure would be negligible (Ref. 9). Exposure from the limited outdoor applications is not expected to be greater than indoor exposure. The limited outdoor use still permitted (application to sidewalks, patios, foundations, and driveways) is expected to present negligible exposure to RAs.

e. *Other applicator exposure estimates.* PCO and RA exposures from total release aerosol foggers, impregnated strips, shelf paper, enclosed or containerized baits, pet dab-ons, and tick and flea collars have not been estimated but are believed to be negligible (Ref. 6).

2. *Post application exposure.* Residents of homes are exposed from post-application exposures, through dermal and inhalation routes of exposure. Home residents may also be exposed while treating household pets.

a. *Crack and crevice study of post-application exposure.* In response to the 1987 DCI, Miles Inc. submitted an acceptable study of post application residential exposure following a crack and crevice and limited structural surface treatment by commercial applicators in five homes using Baygon 70 WP insecticide diluted to a label rate of 1.1 percent a.i. (Ref. 22). The material was applied as a coarse spray to cracks, crevices, baseboards and other areas treated for insect control using a compressed air sprayer. An average of 1.2 oz of a.i. was applied to each house. Surface residues and air levels of propoxur were measured at intervals of up to 48 hours after treatment. Eighteen samples of each of three types of surfaces were monitored: vinyl tile squares represented floors and counters,

nylon carpet squares represented carpet and fabric squares represented furniture. Transferable residues were measured by wiping the sample surfaces with gauze pads. Residue levels from different rooms were pooled for each type of material. The maximum geometric mean of all the measured surface residues for a given surface type was used to represent the measured residue for that surface, at the specified time intervals. Airborne residues were determined by drawing air through a sampling apparatus for 1 hour periods at designated intervals. Exposures were calculated for three age categories of residents: an infant, a 12 year old child, and an adult. The infant was assumed to weigh 7.5 kg, have a body surface area of 4.8 ft², and have a respiratory volume of 0.5 m³/hr. The child was assumed to weigh 40.5 kg, have a body surface area of 14.8 ft², and have a respiratory volume of 0.9 m³/hr. The adult was assumed to weigh 70 kg, have a body surface area of 21 ft², and have a respiratory volume of 1.0 m³/hr. In addition, they were assumed to be exposed 24, 15, and 15 hours/day, respectively. Assumptions about clothing were not specified; rather dermal exposure was expected to occur over 50 percent of the body surface. Individuals were assumed to contact a 50 square foot contact area in a 4-hour interval. Exposure was assumed to occur 365 days/year.

(1) *Crack and crevice*. To calculate exposure following application of wettable powders to cracks and crevices, EPA assumed that 64 oz. of a 1.1 percent solution by weight (total of 0.73 oz.) would be applied once a year for cleanout treatment and 16 oz. of a 0.5 percent solution by weight (total of 0.083 oz.) would be applied 11 times a year for maintenance treatments. Residents were assumed to be exposed 365 days per year over a 70-year lifetime. Dissipation was assumed to be 60 percent, and dermal absorption was assumed to be 50 percent of the residue on skin surfaces, because dermal absorption increases with length of time exposed (Refs. 7, 18, 23, and 24).

To calculate concentrations of propoxur in the air of treated houses, EPA pooled air concentration data for all rooms to yield an average air concentration of 5.1 µg/m³. Absorption by the inhalation route was assumed to be 100 percent. The hours/day of inhalation exposure were the same as for dermal exposure. Total dermal and

inhalation exposure was calculated at 2.8×10^{-4} mg/kg/day (Ref. 23).

EPA realizes exposure could also arise from an oral route. For example, residues could settle on food preparation surfaces or on food. Another potential source of oral exposure could arise from residues on toys or other similar items. In 1989, EPA reviewed the Miles study which measured amounts of propoxur found on surfaces following crack and crevice residential treatment, but the exposure assessment did not address potential oral exposure. At this time EPA does not have a methodology to derive estimates of oral exposure based on residues on these surfaces, food, or toys (Ref. 22). EPA believes that if it were possible to quantify oral exposure resulting from residential use of propoxur, it is unlikely it would greatly change the exposure estimates for this chemical.

(2) *RTU liquids*. Using the wettable powder exposure assessment, EPA also estimated post application exposure following 12 applications per year of a 0.5 percent RTU product by a PCO (Ref. 23). Reducing this exposure threefold, EPA estimated post application exposure following four applications per year of a 0.5 percent RTU liquid propoxur product by an RA. Exposure was estimated at 9.3×10^{-5} mg/kg/day (Ref. 19).

(3) *Aerosols*. Miles Inc. elected not to submit an aerosol spray study for post-application human exposure to aerosol products, so EPA used the post application exposure data from the crack and crevice spray study as a surrogate. EPA adjusted the crack and crevice data to reflect the quantity of a.i. applied during application of a 16 oz. can of 1 percent propoxur aerosol four times per year for 70 years. Total dermal and inhalation exposure was estimated at 5.7×10^{-5} mg/kg/day (Refs. 20 and 25).

(4) *Total release aerosol foggers*. To estimate post application exposure from total release aerosol foggers, EPA used the assumptions of the exposure assessment developed for post application exposure following aerosol use. Thus, the total release aerosol fogger (and also the aerosol) exposure assessment is based on the crack and crevice data. EPA believes it is reasonable to use the crack and crevice data to estimate total release aerosol fogger exposure for the following reasons. First, the crack and crevice study showed that residues are found

throughout the house even though a limited area was treated. A similar distribution of residues would be expected with total release aerosol foggers. Second, the total amount of material released in a total release aerosol fogger is much less than the total amount applied in a crack and crevice application. Third, residues would be deposited on surfaces that people rarely contact, such as ceilings. Exposure (dermal and inhalation) was estimated at 5.7×10^{-5} mg/kg/day (Refs. 6, 20, and 25).

b. *Pest strip study*. After Miles Inc. submitted an unacceptable post application exposure study (Ref. 26), EPA updated a 1985 exposure assessment for impregnated strips. This assessment was based on a study in the technical literature (Ref. 27).

(1) *Pest strips*. EPA assumed that dermal exposure is negligible and 100 percent of propoxur inhaled by the individual is absorbed. Furthermore, the individual was assumed to be exposed 24 hours/day, 365 days/year for 70 years of an average lifetime, and the strips replaced when efficiency diminishes (Refs. 6, 7, and 28). EPA believes these exposure estimates are conservative because the only remaining registrations for pest strips are in areas where human exposure is minimal, such as communications boxes. Inhalation exposure was estimated at 1.1×10^{-4} mg/kg/day.

(2) *Tick and flea collars*. The registrants were not required to submit data on residents' post application exposure to the propoxur found in tick and flea collars. Using data from the impregnated strips study, EPA estimated exposure to residents from surrogate data based on propoxur pest strips (Ref. 26) and dogs. EPA assumed that respiratory absorption is 100 percent, and the exposure is constant over a 70-year lifetime. Inhalation exposure was estimated at 6.3×10^{-6} mg/kg/day (Refs. 6, 7, and 28).

c. *Other post application exposure estimates*. Residents' (including children's) post application exposures from shelf paper, enclosed or containerized baits, and other pet products, including dab-ons and aerosols, have not been estimated but are believed to be negligible (Refs. 6 and 19). EPA believes post application exposure to granular products will not exceed that from aerosol and would probably be much less. (Ref. 9)

TABLE 1.—PROPOXUR USES AND EXPOSURE ESTIMATES FOR PCOs, RAS, KENNEL WORKERS, PET OWNERS, AND RESIDENTS OF TREATED HOMES

Use	Applicator Exposure (mg/kg/day)	Resident Post Application Exposure (mg/kg/day)
Crack and Crevice.		
PCO Application	5.2×10^{-3a}	$2.8 \times 10^{-4a,b}$
RA Application	2.1×10^{-4a}	$9.3 \times 10^{-5a,b}$
Aerosols.		
RA Application	2.1×10^{-4a}	$5.7 \times 10^{-5a,b}$
Granular Baits.		
PCO Application	negligible	negligible
RA Application	negligible	negligible
Pet Aerosols.		
Pet Owner Application	6.4×10^{-3}	negligible
Total Release Aerosol Foggers.		
RA Application	negligible	$5.7 \times 10^{-5a,b}$
Pest Strips.		
RA Application	negligible	1.1×10^{-4}
Shelf Paper.		
RA Application	negligible	negligible
Enclosed or Containerized Baits.		
PCO Application	negligible	negligible
RA Application	negligible	negligible
Pet Dab-ons.		
RA Application	negligible	negligible
Pet Tick and Flea Collars.		
RA Application	negligible	6.3×10^{-6}

^a Dermal absorption is assumed to be 50 percent.^b Dermal contact area is assumed to be 50 sq. ft.

C. Risk Assessment

1. *Non-dietary exposure.* Using the exposure estimates discussed above and the Q_1^* for propoxur, EPA determined the excess lifetime cancer risks to applicators and residents of treated homes. The risks are displayed in Table 2 below. Total residential risks do not exceed the Agency's level of concern. The Agency's policy for applicator risk is that risk should be as close to

negligible as possible. The risk for PCOs applying propoxur to cracks and crevices is 5.4×10^{-6} . Labels require PCOs to wear coveralls, long sleeved shirts, long pants, boots, and chemical resistant gloves. The Agency believes there are no other reasonable protective clothing requirements which can be required to reduce the risk further. Thus, this level of risk is in compliance with the Agency's worker risk policy. In addition, the Agency recently adopted a

policy to incorporate a unified interspecies scaling factor (Ref. 29) when estimating the Q_1^* . This factor adjusts the Q_1^* by a ratio of body surface to body weight. Its exact value depends on the animal test species used. The risks set forth in the following Table 2 have not been calculated using this new scaling factor. If they had, the risk would be approximately one third lower.

TABLE 2.—PROPOXUR USES AND EXCESS LIFETIME CANCER RISKS FOR PCOs, KENNEL WORKERS, RAS, PET OWNERS, AND RESIDENTS OF TREATED HOMES.

Use	Applicator Risk	Resident Post Application Risk	Total Residential Risk ^a
Crack and Crevice.			
PCO Application	5.4×10^{-6}	1.0×10^{-6}	1.0×10^{-6}
RA Application	7.8×10^{-7}	3.4×10^{-7}	1.1×10^{-6}
Aerosols.			
RA Application	7.8×10^{-7}	2.1×10^{-7}	9.9×10^{-7}
Granular Baits.			
PCO Application	negligible	negligible	negligible

TABLE 2.—PROPOXUR USES AND EXCESS LIFETIME CANCER RISKS FOR PCOs, KENNEL WORKERS, RAS, PET OWNERS, AND RESIDENTS OF TREATED HOMES.—Continued

Use	Applicator Risk	Resident Post Application Risk	Total Residential Risk ^a
RA Application	negligible	negligible	negligible
Pet Aerosols.			
Pet Owner Application	2.6×10^{-7}	negligible	2.6×10^{-7}
Total Release Aerosol Foggers.			
RA Application	negligible	2.1×10^{-7}	2.1×10^{-7}
Pest Strips.			
RA Application	negligible	4.1×10^{-7}	4.1×10^{-7}
Shelf Paper.			
RA Application	negligible	negligible	negligible
Enclosed or Containerized Baits.			
PCO Application	negligible	negligible	negligible
RA Application	negligible	negligible	negligible
Pet Dab-ons.			
RA Application	negligible	negligible	negligible
Pet Tick and Flea Collars.			
RA Application	negligible	2.3×10^{-8}	2.3×10^{-8}

^a When application is by PCO, total residential risk includes only risk from post application exposure as the PCO is assumed to have left the treated house. When application is by RA, total residential risk includes both RA risk and post application risk, as the RA is assumed to stay in the treated house.

2. Evaluation of the use of propoxur in food handling establishments.

Propoxur is registered to control pests in food-handling establishments. For example, propoxur products are labeled for crack and crevice application in food areas of food handling establishments. If applications in these areas result in residues of propoxur on food, a food additive regulation would be required to be established under section 409 of the Federal Food, Drug and Cosmetic Act (FFDCA) to cover expected levels of residues on treated food and allow their legal entry into interstate commerce. Miles Inc. filed a petition (9H5199, dated 10/16/78) which stated that crack and crevice applications in food areas of handling establishments resulted in residues on food. Miles, Inc. further proposed a food additive regulation of 0.2 ppm propoxur on all foods.

Section 409 of the FFDCA contains a provision called the Delaney Clause which specifically provides that, with limited exceptions, no additive is deemed safe if it has been found to induce cancer in man or animals. (21 U.S.C. 348(c)(5)).

The Delaney Clause has been interpreted as barring the establishment of food additive regulations for any pesticides that have been found to induce cancer in animals or humans, regardless of the level of risk. (*Les v. Reilly* 968 F2d935 (9th Cir 1992) *Cert Denied*, 113 S. Ct. 1361 (1993).

Because propoxur has been determined to induce cancer within the meaning of the Delaney clause (Ref. 30), the necessary food additive regulation cannot be established. In accordance with EPA's policy and regulations, (see 40 CFR 152.112(g)) requiring coordination of its FIFRA and FFDCA authorities, EPA will propose cancellation of the use of propoxur in food areas of food handling establishments in the near future.

3. *Risk to children.* In 1993 the National Academy of Sciences (NAS) reported on pesticides in the diets of infants and children (Ref. 31). While it did not consider specifically children's risks arising from exposure to propoxur, it raised a number of issues about children's risk from exposure to pesticides in general. This section will discuss some of these issues as they relate to the risk assessment set forth in this document.

a. *Hazard assessment.* The NAS study notes that children may be more or less susceptible to the effects of pesticides. In terms of the propoxur hazard assessment, a question may be raised about whether children metabolize propoxur differently or whether children are more or less sensitive to propoxur's toxic end point—proliferation of urinary bladder epithelial cells. The studies reviewed for the propoxur hazard assessment were largely performed and accepted by

the Agency before the results of the NAS study were available. They do not address these issues. EPA's general approach when addressing gaps in scientific knowledge is to build conservatism into risk assessments to protect children and other sensitive populations. EPA used its conservative (in terms of protecting human health) model of estimating carcinogenic potency. It represents the 95 percent upper bound confidence limit of tumor induction likely to occur from a given dose. EPA has chosen this approach to provide a margin of safety for uncertainties in characterizing the carcinogenic response, for the existence of more sensitive individuals, such as children, in the exposed population and for possible synergism of pesticides and metabolites. For this reason, EPA believes the estimates of cancer risk are conservative. In the review of the toxicology studies in unit II.A. of this document, EPA has noted the possibility that the Carcinogenicity Peer Review Committee may re-evaluate propoxur after all the suggested data have been submitted. EPA does not expect that the peer review will conclude that the carcinogenicity of propoxur is a more serious concern than today's document concludes.

For the future, EPA is taking additional steps to determine whether children are more or less susceptible to the effects of pesticides. EPA is in the

process of planning new research and reviewing its risk assessment methods so that it can better evaluate how these residues affect children.

b. *Dietary exposure.* The NAS Report raised a concern about children's exposure to pesticide residues in the diet. As noted in unit II.C.2. of this document, EPA will propose that the use of propoxur in food handling establishments will be cancelled in the near future.

c. *Non-dietary exposure.* The NAS Report also pointed out that non-dietary sources of pesticides should be considered when estimating total exposure of children. The propoxur exposure assessment considers children and infant's exposure explicitly in assessing post application exposure. For example, the post application exposure assessment considered, for both infants and children separately, different ratios of skin to body weight, different respiratory volumes, and different times spent in a treated house. In terms of the propoxur exposure assessment, a question may be raised about children's exposure to residues from ingested household dust, pets wearing flea collars, or sprayed pets. Presently, EPA does not have a methodology for measuring ingested household dust. EPA believes exposure from flea collars is primarily inhalation, this source of exposure is captured in the exposure assessment, and the risk is small (10^{-8}). Children's exposure to pets treated with aerosol sprays has not been specifically measured. However, the pet owner applicator exposure assessment assumes pets will be treated four times per year for every year of a 70-year lifetime. EPA believes it is unlikely that children will be routinely treating household pets for fleas, and thus believes this exposure estimate is very conservative.

For the future, EPA is initiating a residential research strategy to support development of exposure monitoring and assessment of test guidelines, based on the unique behavior of infants and children, including dermal contact with treated surfaces, hand-to-mouth contact, and object-to mouth contact as well as other modes of exposure. The goal is to develop comprehensive guidelines for assessing exposure to pesticides both inside residences and in other settings, such as yards. EPA would like to set appropriate times for returning to treated residences. The research strategy will also compare exposures of the suburban child and the inner city child who may be exposed to structural pesticide residues carried by ventilation systems. EPA is also working with industry to establish a Task Force to

conduct studies and collect more data on residential exposures.

d. *Children's risk.* Overall, EPA believes the conservative assumptions built into the hazard and exposure assessments have given good estimates of risk to the general population, and in so doing have also been protective of children. EPA is planning additional research in this area. If, in the future, based on new data or methodologies, the risk picture changes, EPA will reconsider this proposed decision not to initiate this Special Review.

D. Unsupported Uses, Risk Reduction, and Amendments to DCIs

No registrant of propoxur end-use products committed to generate trigger pump sprayer data in response to the 1992 DCI. EPA believes that the liquid is likely to drip from the sprayer onto the applicator's fingers, and without data, this exposure and risk cannot be quantified and could be of concern. Accordingly, registrants have either voluntarily cancelled this use pattern or have amended their labels to delete use of ready-to-use liquids with trigger pump sprayers.

IV. Comments Received on the Preliminary Notifications

Comment. In a letter dated March 22, 1988, EPA notified the registrants that it was considering a Special Review of propoxur based on carcinogenicity concerns and the estimated risks posed to PCOs and the general public. In responses dated April 26, 1988 and May 16, 1988, Miles Inc. stated that it already has committed to support the continued registration of propoxur products in response to the 1987 DCI; that EPA should consider all data before deciding on initiating a Special Review of propoxur; and that the bladder carcinogenic effect was species-specific for the rat and Miles Inc. would provide additional data to support its claim. Miles Inc. also urged the Agency not to initiate its Special Review of propoxur without first reviewing the data to be generated by Miles Inc. to satisfy the data requirements outlined in the 1987 propoxur DCI. Also, Miles Inc. suggested that EPA review its cancer classification of propoxur as a Group B2 carcinogen.

Response. EPA has concluded its review of the studies submitted by Miles Inc. to comply with the 1987 DCI. The effects of the voluntary cancellation of and label amendments deleting use of RTU liquids with trigger pump sprayers were considered. EPA has determined that the risks to PCOs and the general public for the remaining registrations of propoxur are likely to present negligible

short-term or long-term human risk. In addition, the registrant has submitted some additional information relating to the carcinogenicity of propoxur. When all the requested data has been submitted, EPA will reconvene a peer review panel to review all the carcinogenicity data relating to propoxur.

V. EPA's Proposed Decision Regarding Special Review

EPA notified propoxur registrants in 1988 that the Agency was considering a Special Review of propoxur. Because of propoxur's Group B2 (probable) human carcinogen classification and wide-spread uses of the pesticide in homes, EPA was concerned with the potential long-term health hazards from prolonged exposures associated with the application of certain indoor formulations. However, since then, EPA has refined the risk assessment. In addition, registrants have cancelled those product registrations and deleted or amended label uses for which EPA had risk concerns. For these reasons, the Agency now concludes that the remaining uses of propoxur products are likely to present negligible short-term or long-term human risk. Therefore, the Agency is proposing not to initiate a Special Review of propoxur at this time.

EPA based its regulatory decision on propoxur entirely on the available information in its exposure database and the result of its risk assessments, which are based on conservative assumptions and the conservative linearized multi-stage model of carcinogenic potency. EPA has concluded that it can issue this regulatory decision in the absence of more conclusive data to resolve the question of diet and species specificity of propoxur in inducing bladder effects in animals, or to resolve the issue on propoxur's suggested activity as a non-genotoxic or "threshold" carcinogen. The Agency believes that the issues surrounding the mechanism of carbamate-induced carcinogenicity are complex, and may be a subject of considerable scientific debate for the future.

VI. Executive Order 12898 on Environmental Justice

In accordance with the Executive Order on Environmental Justice, EPA has reviewed this proposed decision and found it does not result in any adverse environmental effects (including human health, social and economic effects) on minority communities and low-income communities.

VII. Public Record and Opportunity for Comment.

EPA has established a public docket (OPP-30000/59) for the propoxur Pre-Special Review. This public record includes: (1) this Notice; (2) any other notices pertinent to the propoxur Special Review; (3) non-Confidential Business Information (CBI) documents and copies of written comments submitted to EPA in response to the pre-Special Review registrant notification, (4) any other Notice regarding propoxur submitted at any time during the Pre-Special Review process by persons outside government; (5) a transcript of all public meetings held by EPA for the purpose of gathering information on propoxur; (6) memoranda describing each meeting held on propoxur between EPA personnel and persons outside government during the Pre-Special Review process; and (7) a current index of materials in the public docket. Additional information about the docket may be found in the section on addresses at the beginning of this notice.

EPA is providing a 60-day period for registrants, applicants, and interested persons to comment on the risks associated with indoor and pet uses of propoxur products, and on EPA's proposed decision not to initiate a Special Review of propoxur. Written comments must be submitted by March 14, 1995, and must be identified by the docket number (OPP-30000/59). Comments should be sent to the address provided at the beginning of this notice.

VIII. References

The documents referred to in this Notice are listed below. Copies are available in the Public Docket. Information about the Public Docket is available in the ADDRESSES unit at the beginning of this notice.

(1) Letter from D. Campt, Director, Office of Pesticide Programs, to propoxur registrants, dated March 22, 1988.

(2) Eben, A. "Studies on Transformation of Propoxur in Humans," dated June 1, 1987, Accession Number 406297-4, Data Evaluation Report (DER) No. 6858.

(3) Memorandum from B. Fisher, HED, to B. Backus, HED, titled Propoxur (Baygon) Qualitative Risk Assessment, Revised and Quantitative Risk Assessment—Two-Year SPF Rat Dietary Study, dated April 21, 1992.

(4) Memorandum from D. Jaquith, HED, to D. Edwards, RD, titled Review of Propoxur Exposure Studies Submitted by Mobay Corporation in Response to Data-Call-In Notice (HED Project Nos. 9-1935, 9-1936, 9-1937, 9-1938, 9-1939) and Current Estimates of Exposure for Other Scenarios, dated February 7, 1990.

(5) Memorandum from E. Budd, HED, to J. Gallagher, SRRD, titled Propoxur: Carcinogenic Risk Assessment for Pest Control Operators Treating Indoor Sites (Utilizing Dermal Absorption Data) (Crack

and Crevice Study) dated January 24, 1991, updated August 14, 1992.

(6) Memorandum from E. Budd, HED, to D. Chen, SRRD, titled Propoxur: Quantitative Risk Assessments for Remaining End-Use Formulations Listed in OREB Memorandum of November 6, 1992, dated February 8, 1993.

(7) Memorandum from D. Jaquith, HED, to D. Chen, SRRD titled Refinement of Exposure Analysis for Propoxur, dated November 6, 1992.

(8) Memorandum from D. Jaquith, HED, to D. Edwards, RD, titled Review of Repeated Exposure Study Addressing Application of a 2 percent propoxur bait (HED Project No. 1-1471) dated November 15, 1991.

(9) Memorandum from D. Jaquith, HED, to A. Sibold, SRRD, titled Exposures to Propoxur from Granular Baits Applied in and around Homes dated May 24, 1994.

(10) Memorandum from D. Jaquith, HED, to D. Edwards, RD, titled Review of Repeat Exposure Study for Propoxur Pet Spray Products (HED Project No. 2-0491) dated July 15, 1992.

(11) Memorandum from Byron Backus, HED, to McCall/Whitby, HED, titled Used of Measurements of 2-Isopropoxyphenol in Human Urine Samples to Determine Exposure and Absorption of Propoxur, dated June 28, 1994.

(12) Memorandum from David Jaquith, HED, to Deborah McCall, HED, titled Response to Questions from SRB Regarding Propoxur, dated July 13, 1994.

(13) Memorandum from E. Budd, HED to D. Chen, SRRD, titled Propoxur: Carcinogenic Risks for Individuals Apply a 0.25 Percent Aerosol Spray to Pets. dated August 14, 1992.

(14) Memorandum from Deborah McCall, HED to Ann Sibold, SRRD, titled Propoxur: Revisions to Carcinogenic Risk Estimates for Commercial Workers and Homeowners Exposed to Pet Sprays, dated July 25, 1994.

(15) Memorandum from D. Jaquith, HED, to D. Chen, SRRD, titled Review of Repeat Exposure Study for Propoxur Aerosol Spray (HED Project No. 1/1208), dated July 29, 1991.

(16) Memorandum from K. Whitby, HED, to D. Chen, SRRD, titled Propoxur (Baygon) Carcinogenic Risk for Homeowners Applying 1 percent Aerosol Spray Products, dated September 1, 1992.

(17) Memorandum from D. Jaquith, HED, to D. Chen, SRRD, titled Classification of Propoxur Use Sites and Expansion of Exposure Matrix for Aerosol Uses, dated August 11, 1992.

(18) Memorandum from D. Jaquith, HED, to D. Chen, SRRD, titled Errors in Exposure Analysis for Propoxur, dated November 18, 1992.

(19) Memorandum from Deborah McCall, HED, to Ann Sibold, SRRD, titled Propoxur: Revised Lifetime Risk Numbers for Ready-to-Use Sprays, dated August 12, 1994.

(20) Memorandum from D. Jaquith, HED, to D. Chen, SRRD, titled Post-Application Exposures of Residents to Propoxur Applied as an Aerosol Spray, dated November 1, 1991.

(21) Memorandum from David Jaquith, HED, to Deborah McCall, HED, titled Clarification of Resident Applicator Exposures from Ready to Use (RTU)

Formulations of Propoxur, dated August 5, 1994.

(22) Memorandum from D. Jaquith, HED, to D. Edwards, RD, titled Review of Study Estimating Resident Exposure to Propoxur Following Crack and Crevice Treatment (HED project No. 9-1936) dated November 15, 1989.

(23) Memorandum from E. Budd, HED, to D. Chen, SRRD, titled Propoxur: Revised Carcinogenic Risk Assessment for Residents of Homes Following Crack and Crevice Treatments (Utilizing Refined Exposure Analysis Provided OREB in Memoranda of November 6, 1992 and November 18, 1992), dated December 8, 1992.

(24) Memorandum from D. Jaquith, HED, to J. Gallagher, SRRD, titled Adjustments to Post Application Exposure Assessment for Residents of Homes treated with Propoxur (HED Proj. No. 1-0222), dated February 27, 1991.

(25) Memorandum from E. Budd, HED, to D. Chen, SRRD, titled Propoxur: Revised Carcinogenic Risk Assessment for Residents of Homes Following Treatments with a 1 percent Aerosol Product (Utilizing Refined Exposure Analysis Provided by OREB in Memoranda of 11/6/92 and 11/18/92), dated December 8, 1992.

(26) Memorandum from S. Knott, HED, to D. Edwards, RD, titled review of Post Application Exposure from Indoor Pest Strips Containing Propoxur (HED Project No. 9-1540) dated August 2, 1989.

(27) Jackson, M.D. and Lewis, R.G., (1981) Insecticide Concentrations in Air after Application of Pest Control Strips. Bull Environm Contam Toxicol 27:122-125.

(28) Memorandum from C. Lunchick, EAB, to Jay Ellenberger, RD, and Robert Zendzian, HED, titled Exposure Assessment for Propoxur (Baygon) dated January 8, 1985.

(29) Memorandum from Penelope Fenner-Crisp, HED, to Bill Burnam, Hugh Pettigrew, and Kerry Dearfield, titled Deriving Q*s Using the Unified Interspecies Scaling Factor, dated July 8, 1994.

(30) Memorandum from Stephanie Irene, HED to Louis P True, Jr., SRRD, and Stephen Johnson, RD, titled Propoxur - Carcinogenicity in Animals, dated December 14, 1994.

(31) National Research Council (U.S.). Committee on Pesticides in the Diets of Infants and Children, Pesticides in the Diets of Infants and Children. copyright 1993 by the National Academy of Sciences.

List of Subjects

Environmental protection, chemicals, pesticides and pest.

Dated: December 30, 1994.

Lynn R. Goldman,

Assistant Administrator for Prevention, Pesticides and Toxic Substances.

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